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EXAMINER

HUTSON, R

ART UNIT	PAPER NUMBER
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1652

12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/258,031

Applicant

Stulver et al.

Examiner

Richard Hutson

Group Art Unit
1652



☒ Responsive to communication(s) filed on Feb 25, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-50 is/are pending in the application

Of the above, claim(s) 7-10, 12-38, 42-44, and 46-50 is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-6, 11, 39-41, and 45 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims 1-50 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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DETAILED ACTION

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-12, 39-41 and 45, drawn to carbohydrate oxidase protein which has antifungal activity, classified in class 435, subclass 190.
- II. Claims 13-17, 18-31, 32-37 and 47-49, drawn to a DNA encoding a carbohydrate oxidase protein which has antifungal activity, classified in class 435, subclass 190.
- III. Claims 38 and 42, drawn to a method of retarding fungal growth, classified in class 424, subclass 94.4.
- IV. Claims 43-44, drawn to method for obtaining plants with reduced susceptibility to fungi, classified in class 800, subclass 279.
- V. Claim 46, drawn to an antibody capable of recognizing a carbohydrate oxidase with antifungal activity, classified in class 530, subclass 387.1.
- VI. Claim 50, drawn to a method of making a plant expressible gene construct using the DNA that encodes a carbohydrate oxidase protein which has antifungal activity, classified in class 435, subclass 91.4.

The inventions are distinct, each from the other because of the following reasons:

Inventions I, II and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different

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functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, the DNA of Group II, the protein of Groups I and the antibody of Group V each comprise a chemically unrelated structure capable of separate manufacture, use and effect. The DNA comprises a nucleic acid sequence and the proteins of Groups I and V each comprise an unrelated amino acid. The DNA has other utility besides encoding the proteins such as a hybridization probe, the proteins can be made by another method such as isolation from natural sources or chemical synthesis and the proteins have other utility besides acting as an antigen to induce the antibodies such as for use as antifungal agents.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the product can be used to induce the antibodies of Group V.

The DNA of Group II and the antibody of Group V are unrelated to the method of Group III as they are neither used nor made by the method of Group III.

Inventions II and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the product can be used as a diagnostic or a hybridization probe.

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The protein of Group I and the antibody of Group V are unrelated to the method of Group IV as they are neither used nor made by the method of Group IV.

Inventions II and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the product can be used as a diagnostic or a hybridization probe.

The protein of Group I and the antibody of Group V are unrelated to the method of Group VI as they are neither used nor made by the method of Group VI.

The methods of Groups III, IV and VI are independent as they comprise different steps, utilize different products and produce different results.

Because these inventions are distinct for the reasons given above and the search required for Groups I-VI is not coextensive, restriction for examination purposes as indicated is proper.

"For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP 808.02." (see MPEP 803).

This application contains claims directed to the following patentably distinct species of the claimed invention: A carbohydrate oxidase having antifungal activity from Sunflower, Lettuce and *Arabidopsis*.

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Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-5, 13, 22-38 and 41-50 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Clifford Mass on 2/17/2000 a provisional election was made with traverse to prosecute the invention of group I, claim 1-12, 39-41 and 45 drawn to the species of Sunflower. Affirmation of this election must be made by applicant in replying to

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this Office action. Claims 7-10, 12-38, 42-44 and 46-50 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by

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"such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1-3 recite the broad recitation "which has antifungal activity", and the claims also recite "preferably anti-Oomycete activity, and more preferably anti-Phytophthora and/or anti-Pythium activity" which is the narrower statement of the range/limitation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 11, 39-41 and 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2, 5, 6 and 11 are directed to all possible proteins having antifungal activity, wherein said encoded by a specific nucleotide sequence as listed or parts or **muteins** thereof (claims 5, 6 and 11) wherein said protein is obtainable from a plant (claim 1) such as sunflower (claim 2), or antifungal compositions comprising said proteins (claim 45). Claims 3 and 4 are

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directed to all possible carbohydrate oxidase proteins (claim 4) wherein said protein having antifungal activity (claim 3). Further, claims 39-41 are directed to **any** plant derived protein having a molecular weight of 55-65 kD and carbohydrate oxidase activity (claim 39), specifically any hexose oxidase (claim 40), wherein said hexose oxidase is from sunflower (claim 41). The specification, however, only provides representative species from sunflower, lettuce and *arabidopsis* encompassed by these claims. There is no disclosure of any particular **structure to function/activity** relationship in the disclosed species. The specification also fails to describe additional representative species of these proteins by any identifying structural characteristics or properties other than the carbohydrate oxidase activity and antifungal activity, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would not recognize Applicants were in possession of the claimed invention.

Claims 1-6, 11, 39-41 and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those carbohydrate oxidase proteins having antifungal activity wherein the proteins are encoded by the nucleotide sequence as shown in SEQ ID NOs: 15, 19, or comprising peptides selected from the group consisting of SEQ ID NOs: 1, 2, 6, 16 and 20, does not reasonably provide enablement for any protein having carbohydrate oxidase or antifungal activity, wherein said protein is encoded by a specific nucleotide sequence as claimed or parts or **muteins** thereof, wherein said protein is obtainable from a plant such as sunflower, or

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antifungal compositions comprising said proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-6, 11, 39-41 are so broad as to encompass any protein having antifungal activity, wherein said protein is encoded by a specific nucleotide sequence as claimed or parts or **muteins** thereof (claims 5, 6 and 11) wherein said protein is obtainable from a plant (claim 1) such as sunflower (claim 2), or antifungal compositions comprising said proteins (claim 45). Claims 3 and 4 are so broad as to encompass any carbohydrate oxidase protein (claim 4) wherein said protein has antifungal activity (claim 3). Further, claims 39-41 are so broad as to encompass **any** plant derived protein having a molecular weight of 55-65 kD and carbohydrate oxidase activity (claim 39), any hexose oxidase (claim 40), and any hexose oxidase from sunflower (claim 41). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to those carbohydrate oxidase proteins having antifungal activity wherein the proteins are encoded by the

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nucleotide sequence as shown in SEQ ID NOs: 15, 19, or comprising peptides selected from the group consisting of SEQ ID NOs: 1, 2, 6, 16 and 20.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any carbohydrate oxidase or antifungal protein because the specification does not establish: (A) regions of the protein structure which may be modified without effecting these activities; (B) the general tolerance of these carbohydrate oxidase and antifungal proteins to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any carbohydrate

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oxidase or any antifungal protein. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those proteins having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 3, 4, 5, 6, 11 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Stougaard et al. (WO 96/40935).

Stougaard et al. teach a method of producing recombinantly a hexose oxidase from a number of different marine algal species for use as an antimicrobial agent. Specifically, Stougaard et al. teach the use of hexose oxidase as expressed in silage inoculants to deplete oxygen thereby inhibiting the growth of aerobic spoilage organisms such as gram negative bacteria and yeasts (page 16, lines 12-32).

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Therefore, Stougaard et al. anticipates claims 1, 3, 4, 5, 6, 11 and 45, drawn to an isolated protein which has antifungal activity, carbohydrate oxidase activity, which is obtainable from a plant source encoded by the nucleotide sequence shown in SEQ ID NO: 15 or a **mutein thereof**, has an amino acid sequence according to SEQ ID NO: 16 or a **mutein thereof** and a antifungal composition containing said protein.

Claims 1, 5, 6, 11 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Hu et al. (Plant Molecular Biology 34: 949-959, Aug 1997).

Hu et al. teach the cloning and expression of a PR5-like protein from *Arabidopsis*, its expression in *E. coli* and its use to inhibit fungal growth as part of a composition.

Therefore Hu et al. anticipates claims 1, 5, 6, 11 and 45.

Claims 1, 5, 6, 11 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Woloshuk et al. (Plant Cell 3: 619-628, June 1991).

Woloshuk et al. teach that the cell walls of most fungi in the taxonomic class Oomycetes have a β -1,3-glucan component but contain no chitin, thus the Oomycetes *Phytophthora cactorum*, *Pythium ultimum*, and *Pythium aphanidermatum* have been shown to be insensitive to a mixture of chitinase and β -1,3-glucanase. Woloshuk et al. further hypothesize that factors other than chitinase and β -1,3-glucanase are involved in induced resistance against this class of pathogens. Woloshuk et al. teach a bioassay using *P. infestans* for the identification of the factors involved in the resistance to this agronomically important pathogen. Woloshuk et al. further identified,

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purified and characterized a protein, AP24 from tobacco plants, which caused lysis of sporangia and inhibition of hyphal growth.


Therefore, Woloshuk et al. anticipates claims 1, 5, 6, 11 and 45.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on M-F from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapy Achutamurthy (Murthy), can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson
4/20/2000


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